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09/902,693	07/12/2001	Yasuhiro Mihara	211110US0DIV	3140

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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER

NGUYEN, QUANG

ART UNIT	PAPER NUMBER
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1636

15

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/902,693

Applicant(s)

MIHARA ET AL.

Examiner

Quang Nguyen, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 19 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-20 and 22-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-20 and 22-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/347,001.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/19/03 has been entered.

Amended claims 17-20 and 22-25 are pending in the present application, and they are examined on the merits herein.

Response to Amendments

The terminal disclaimer filed on March 19/2003 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent No. 6,335,177 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Accordingly, the rejection of claims 17-20 and 22-25 under obviousness-type double patenting is withdrawn.

Following is a new ground of rejection.

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Written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claims 17-19 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

Applicant's invention is drawn to a method for producing xylitol or D-xylulose from glucose utilizing a bacterium whose evolutionary distance is not more than the evolutionary distance between *Acetobacter methanolicus* and *Acetobacter pasteurianus*, including one that belongs to the genus *Asaia*, and more specifically belongs to *Asaia ethanolifaciens*. Applicant's invention is also drawn to a method for producing xylitol or D-xylulose from glucose utilizing a bacterium whose evolutionary

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distance is not more than the evolutionary distance between *Gluconobacter oxydans subsp. oxydans* and *Acetobacter aceti*, including one that belongs to the genus *Zucharibacter*, and more specifically belongs to *Zucharibacter floricola*. The specification identifies and characterizes five microbial strains that have the ability to produce xylitol or D-xylulose from glucose in cell cultures, four of which (S877, S1009, S1019 and S1023 strains) are designated in a new genus *Zucharibacter floricola* and the other (P528 strain) is assigned to a new genus *Asia ethanolifaciens* by Applicants. The instant claims embraced a method for producing xylitol or D-xylulose from glucose using any bacterium as long its evolutionary distance is not more than the evolutionary distance between *Acetobacter methanolicus* and *Acetobacter pasteurianus* or more than the evolutionary distance between *Gluconobacter oxydans subsp. oxydans* and *Acetobacter aceti*, and that it has the functional limitations recited in the claims, including bacteria that exist in nature and yet have not been isolated. Apart from the functional limitations and generic limitations on the quinone type and GC content of DNA, there is no common essential core structure or elements that are shared between the strains P528, S877, S1009, S1019 and S1023 identified in the instant specification to a broad genus of bacterium encompassed by the instant claims. There is also no apparent relationship between the evolutionary distance of the bacterium with the common essential core structure or elements to be shared by members of a broad genus of bacterium contemplated by Applicants to be used in the methods as claimed. For example, the evolutionary distance between the strain P528 and *Acetobacter pasteurianus* (0.0419, see instant specification page 30, line 5) is even greater than the

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distance between two distinct genera *Gluconobacter* and *Acetobacter* (0.044, line 27 of page 29 continues to line 1 of page 30). The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants' filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). Since the five isolated microbial strains disclosed in the instant specification represent only a small portion of the total number of strains in a family or in a genus encompassed by the instant claims, Applicants have not possessed a representative number of species of strains to describe the broad genus or a family of bacterium that is being utilized in the claimed methods. Particularly, the identification of a single bacterial strain P528 is not a reasonable representative for the whole genus of *Asaia ethanolifaciens* or *Asaia*. The phenotype of one strain from a species of a genus of thousands of bacteria is not representative of the genus as a whole, let alone for any bacterium whose evolutionary distance is not more than the evolutionary distance between *Acetobacter methanolicus* and *Acetobacter pasteurianus*.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co.*

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Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Response to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on March 19, 2003 in Paper No. 14 (page 5) have been fully considered.

Applicants argue mainly that the bacterium in the amended claims is defined not only by an evolutionary distance calculated by CLUSTAL W based on the 16S rRNA nucleotide sequences, but also by biochemical and physiological characteristics recited in the claims, and therefore the instant specification meets the Written Description requirements for a bacterium to be utilized in the methods as claimed.

Applicants' arguments are respectfully found unpersuasive because there is no apparent relationship between the evolutionary distance of a bacterium with the common core structure or elements or desired phenotypes to be shared by members of a broad genus of bacterium contemplated by Applicants to be utilized in the methods as claimed. For example, the evolutionary distance between the strain P528 and *Acetobacter pasteurianus* (0.0419, see instant specification page 30, line 5) is even greater than the distance between two distinct genera *Gluconobacter* and *Acetobacter* (0.044, line 27 of page 29 continues to line 1 of page 30). Additionally, the recited

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functional limitations (e.g., ability to produce xylitol or D-xylulose from glucose, an ability to produce acetic acid from ethanol, grows in the presence of 30% glucose) are not structural characteristics but are desired functional properties for which no common structural features have been described. Nor do the generic limitations of the quinone type and GC content of DNA (shared or encompassed by other distinct bacterial genera, see Table 9 of the instant specification) define sufficient relevant identifying characteristics for a broad genus of bacterium that is being utilized in the methods as claimed. Furthermore, at the effective filing date of the present application, Applicants have not possessed a representative number of species of bacterial strains for a broad genus of bacterium contemplated by Applicants to practice the methods as claimed. The identification of a single bacterial strain P528 is not a reasonable representative for the whole genus of *Asaia ethanolifaciens* or *Asaia*. The phenotype of one strain from a species of a genus of thousands of bacteria is not representative of the genus as a whole. Similarly, the four disclosed microbial strains from *Zucharibacter floricola* do not fairly represent a broad spectrum of the genus because these microbial strains could all be clustered at one end of the spectrum for such a genus. It is noted that the method claims require essential or critical elements, for this instance representative microbial species representing the broad genus of bacterium encompassed by the claims, which are not adequately described in the specification and which are not conventional in the art as of Applicants' filing date. Additionally, adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method

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of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

Accordingly, claims 17-19 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth above.

Following is a new ground of rejection.

Claim Rejections - 35 USC § 112

Amended claims 17-20 and 22-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing xylitol or D-xylulose, which comprises: culturing a bacterium having an ability to produce xylitol or D-xylulose from glucose in a suitable medium to accumulate xylitol or D-xylulose in the medium, and collecting xylitol or D-xylulose from the medium, wherein said bacterium is the isolated microbial strain P528, S877, S1009, S1019 or S1023, does not reasonably provide enablement for a method for producing xylitol or D-xylulose from glucose using a bacterium as recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Amended claims 17-20 are drawn to a method for producing xylitol or D-xylulose from glucose in a culture utilizing a bacterium whose evolutionary distance is not more than the evolutionary distance between *Acetobacter methanolicus* and *Acetobacter pasteurianus*, including one that belongs to the genus *Asaia*, and more specifically

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belongs to *Asaia ethanolifaciens*, or one that has a 16S rRNA gene comprising the nucleotide sequence of SEQ ID NO:1.

Claims 22-25 are directed to a method for producing xylitol or D-xylulose from glucose utilizing a bacterium whose evolutionary distance is not more than the evolutionary distance between *Gluconobacter oxydans* subsp. *oxydans* and *Acetobacter aceti*, including one that belongs to the genus *Zucharibacter*, and more specifically belongs to *Zucharibacter floricola*, or one that has a 16S rRNA gene comprising the nucleotide sequence of SEQ ID NO:2, 3, 4 or 5.

The specification teaches the isolation and partial characterization of isolated microbial strains P528, S877, S1009, S1019 and S1023. Among the 3000 strains isolated and cultured, the aforementioned strains possess the biochemical characteristics or properties as claimed (e.g., producing xylitol or D-xylulose from glucose in cell cultures). The specification further teaches that upon analysis of the 16 rRNA nucleotide sequences for the isolated strains P526 and S877, and partial 16 rRNA sequencing analysis for strains S1009, S1019 and S1023, coupled with multiple alignment and evolution distance calculation for the obtained sequences with analogous bacterial sequences available from databases, a molecular phylogenetic tree was established. As a result, the strain P528 was identified as a new species belonging to the genus *Asaia*, and provisionally designated by Applicants as *Asaia ethanolifaciens* sp. nov. The strains S877, S1009, S1019 and S1023 were all identified as microorganisms of a new species belonging to a new genus, and provisionally designated by Applicants as *Zucharibacter floricola* gen. No., sp. nov. The above

evidence has been noted and considered. However, the evidence is not reasonably extrapolated to the instant broadly claimed invention for the following reasons.

(1) The breadth of the claims. The instant claims encompass a method for producing xylitol or D-xylulose in culture utilizing any bacterium whose evolutionary distance is not more than the evolutionary distance between *Acetobacter methanolicus* and *Acetobacter pasteurianus*, including one that belongs to the genus *Asaia*, and more specifically belongs to *Asaia ethanolifaciens*, or one that has a 16S rRNA gene comprising the nucleotide sequence of SEQ ID NO:1; as well as utilizing any bacterium whose evolutionary distance is not more than the evolutionary distance between *Gluconobacter oxydans subsp. oxydans* and *Acetobacter aceti*, including one that belongs to the genus *Zucharibacter*, and more specifically belongs to *Zucharibacter floricola*, or one that has a 16S rRNA gene comprising the nucleotide sequence of SEQ ID NO:2, 3, 4 or 5.

(2) The state and the unpredictability of the prior art. At about the effective filing date, species of bacterial strains having the properties required by the methods as claimed are not available in the prior art. As a result of the present invention, the single strain P528 was identified as a new species belonging to the genus *Asaia*, and provisionally designated by Applicants as *Asaia ethanolifaciens sp. nov.* The strains S877, S1009, S1019 and S1023 were all identified as microorganisms of a new species belonging to a new genus, and provisionally designated by Applicants as *Zucharibacter floricola gen. No., sp. nov.* Additionally, there is no apparent relationship between the evolutionary distance of a bacterium with the common core structure or elements or

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desired phenotypes to be shared by members of a broad genus of bacterium contemplated by Applicants to be utilized in the methods as claimed. For example, the evolutionary distance between the strain P528 and *Acetobacter pasteurianus* (0.0419, see instant specification page 30, line 5) is even greater than the distance between two distinct genera *Gluconobacter* and *Acetobacter* (0.044, line 27 of page 29 continues to line 1 of page 30). Furthermore, there is no apparent relationship that any bacterium containing a 16S rRNA gene having the nucleotide sequence of SEQ ID NO:1, 2, 3, 4, or 5 would necessarily possess all the properties required by the methods as claimed. Therefore, it would have required undue experimentation for a skilled artisan to test every single bacterium on a trial-error basis to select the bacterium possessing the recited limitations to be utilized in the methods as claimed.

(3) The amount of direction or guidance provided. Apart from the disclosure of a single isolated bacterial strain P528 newly designated to *Asaia ethanolifaciens* and four closely related bacterial strains S877, S1009, S1019 and S1023 newly designated to *Zucharibacter floricola*, neither the prior arts at the effective filing date of the present application nor the instant specification provide sufficient guidance for a skilled artisan on how to obtain other related bacterial species or related genus having the desired functional characteristics. It is unclear whether the four disclosed microbial strains from *Zucharibacter floricola* represent a broad spectrum of the genus or that they are all clustered at one end of such a genus. The identification of a single bacterial strain P528 is not a reasonable representative for the whole genus of *Asaia ethanolifaciens* or *Asaia*. The phenotype of one strain from a species of a genus of thousands of bacteria

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is not representative of the genus as a whole. Moreover, it is unclear whether the soil samples collected from the bank of Tama river or at any other locations or other non-soil samples contain a sufficient number of related bacterial species to represent broad bacterial genera to be utilized in the methods as claimed. Therefore, it would have required undue experimentation for a skilled artisan to practice the full scope of the instant broadly claimed invention, particularly with regard to the amount of experimentation required to screen a large number of bacterial strains representative of the broad genus of bacterium on a trial-error basis for the practice of the methods as claimed.

With respect to the breadth of the presently claimed invention, Applicants are directed to the decision *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; *In re Wahlforss et al.*, 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

Additionally, the courts have also stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in the patent application (27 USPQ2d 1662 *Ex parte Maizel*.).

Accordingly, due to the lack of sufficient guidance provided by the specification on the issues discussed above, the quantity of experimentation necessary, the state of the prior art, and the breadth of the claims, it would have required undue

experimentation for one skilled in the art to make and use the instant broadly claimed invention.

Response to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on March 19, 2003 in Paper No. 14 (page 6) have been fully considered.

Applicants argue mainly that one skilled in the art is capable of screening the claimed bacterium based on the present specification and the knowledge in the art.

Applicants' argument is respectfully found unpersuasive because in the absence of the availability of representative number of species of strains or genus of related species provided by the present invention or in the prior art at the effective filing date of the present application, it would have required undue experimentation for a skilled artisan to practice the full scope of methods as claimed, particularly with regard to the amount of experimentation required to screen a large number of bacterial strains on a trial-error basis so that the selected bacterium has the recited limitations. It should be noted that the courts have also stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in the patent application (27 USPQ2d 1662 *Ex parte Maizel*.).

Accordingly, claims 17-20 and 22-25 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth above.

Conclusions

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No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Gerald Leffers, Jr., Ph.D., may be reached at (703) 305-6232, or SPE, Remy Yucel, Ph.D., at (703) 305-1998.

Quang Nguyen, Ph.D.

Gerald B. Leffers Jr.
PATENT EXAMINER
Gerald B. Leffers Jr.